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Associations between pre-operative radiographic changes and outcomes after total knee joint replacement for osteoarthritis

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SUMMARY

Objective: To assess the influence of pre-operative X-ray changes on the response to total knee joint replacement (TKR).
Methods: We included patients from one centre who underwent primary TKR ($n = 478$) for osteoarthritis in 2006 and 2007. The International Knee Society Score (IKSS) and Short Form Health Survey were collected pre-operatively and at 1 and 2 years after surgery. Pre-operative radiographs were read to assess Kellgren and Lawrence (K–L) grading, individual radiographic features using the OARSI atlas, and subchondral bone attrition using the Ahlbach method.
The main independent variable was a modified (K–L) grade. The outcome variables were the IKSS pain and function scores. Covariates included demographic features, co-morbidities, baseline pain and function, prosthesis type, and the use of patella resurfacing. Multivariable linear regression models were created to assess the relationships between pre-operative X-ray findings and pain and function outcomes.
Results: On average, pain and function improved greatly following surgery. However, pain relief was unsatisfactory in about 30%, and functional improvement suboptimal in about 50%. OR (95% CI) for ongoing moderate-severe pain at 12 months for modified K–L grades; <3: 5.39 (1.23–15.69), 3a: 2.62 (1.21–5.67), 3b: 1.81 (1.00–3.26), 4a: 2.06 (1.05–4.05) when compared to 4b. OR (95% CI) for poor function at 12 months were; 3a: 2.81 (1.23–6.39) and 4a: 2.45 (1.22–4.91), when compared to 4b.
Conclusions: Patients with more severe radiographic knee damage at the time of surgery are most likely to have substantial gains in terms of both pain relief and improved function as a result of a TKR.

Introduction

Total knee joint replacement (TKR) is an effective and cost-effective intervention for people with advanced osteoarthritis (OA) of the knee[1,2]. Many studies have confirmed the beneficial impact of TKR on pain, disability and quality of life[3,4]. As a result of these data, all guidelines on the management of knee OA recommend TKR for severe disease[5]. The prevalence of knee OA is increasing alarmingly in Western societies as people become older and more obese[6,7], so that the numbers of TKRs being done each year is also increasing[8].

However, not everyone experiences a health gain as a result of a TKR. In the immediate post-operative period, there is a small but important risk of severe complications[9–11]; after 10 or more years there is the risk of prosthesis loosening or failure resulting in the need for complex revision surgery[12]. In the intermediate period (6 months–10 or more years), most people can expect improvements in pain and disability. However, there is an important minority who do not achieve such gains. A recent systematic review of the long-term pain outcome after knee replacement reported an unfavourable outcome in about 20% of patients[13].

The reasons for these poor outcomes after TKR are not clear. Recent work has identified a number of risk factors for continuing

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pain and disability after TKR; these include: more severe pain and disability pre-operatively, anxiety and depression, age, co-morbidities, obesity, and patient expectation[3,10,14–18]. However, these variables can only account for a minority of the variance in outcomes observed, suggesting that other risk factors must be important[19]. Given the increasing numbers of TKRs performed, understanding more about the determinants of good and bad outcomes is an imperative.

A few recent studies have suggested that those with less severe radiographic change are less likely to respond well to TKR[20,21] and this is in keeping with the literature on a number of other procedures such as surgery for disc herniation[22] and spinal canal stenosis[23]. However, studies to date in TKR have methodological limitations and have only used crude measures of overall radiographic severity of the disease, rather than individual radiographic features and the compartmental distribution of OA.

The purpose of this study was to evaluate the prognostic value, of pre-operative radiographic characteristics such as compartmental involvement, articular cartilage loss [joint space narrowing (JSN)], new bone formation (osteophytosis) and loss of bone (bone attrition) on the pain and disability experienced by people 1 and 2 years after TKR.

Methods

Ethics approval

This study was approved by the Human Research Ethics Committee of St. Vincent's Hospital (SVH) Melbourne, and informed consent was obtained from participants.

Study institution and patients

This study was conducted at SVH, in Melbourne, Australia. All patients with OA admitted to SVH who underwent primary TKR between 1 January 2006 and 31 December 2007 were considered eligible for enrolment into the study, and only four declined to participate. Patients attended a multidisciplinary pre-admission clinic within 8 weeks of surgery, which served as the baseline for our study.

Data collection

Baseline data was prospectively collected and included patient demographics (age, sex, BMI), the surgeon's diagnoses, and self-reported co-morbidities. Follow-up captured an extensive range of outcomes, including surgery and prosthesis related variables.

One condition-specific questionnaire (International Knee Society Score – IKSS)[24] and one general health questionnaire (Short Form Health Survey – SF12)[25] were completed at the baseline visit and at 12 and 24 months post-operatively. The previously validated pain and function scores were derived from the IKSS[26,27], and from the SF12[28], both the physical (PCS) and mental (MCS) component scores were determined. Post-operative questionnaires were mailed to patients with instructions to complete and bring with them to their scheduled follow-up appointments. Questionnaires were collected by clinic staff. Additional mail-outs were also completed for non-responders followed by a phone call 4 weeks later for any incomplete data or missing surveys.

Radiographs

Radiographs taken within 6 months of surgery were assessed by a single observer (PD), who was blinded to outcome scores. To assess the tibio-femoral joint, full-leg, weight-bearing, antero-posterior (AP) views were obtained and a lateral or skyline view was available to assess the patella-femoral joint. Long-leg films were obtained using a set of three 43 cm $\times$ 36-cm cassettes with a graduated grid. The lower limbs were fully extended and positioned on a custom-made Perspex footrest that allowed the tibial tuberosities to face forward and the lateral malleoli to be 30 cm apart, as described previously[29].

Intra-observer error was assessed by reading 50 randomly selected films twice, in random order, 1 week apart. Differences were assessed using the kappa statistic[30].

Data recorded from AP films included Kellgren and Lawrence (K–L) grading (0–4)[31], the severity of JSN (0–3) and osteophyte formation (0–3) using the Osteoarthritis Research Society International (OARSI) atlas[32], and the degree of bone attrition using a previously described method (Dieppe *et al*.., 2005). Radiographs showing advanced OA, (K–L grades 3 and 4) were further subdivided by including data from the individual scores of JSN and bone attrition as described previously for the hip[33]. In this modified K–L grading system (mK–L), a K–L grade 3 radiograph with mild JSN (1) was graded 3a, and one with more severe JSN (2) 3b. A K–L grade 4 radiograph (complete loss of joint space = 3) was divided into 4a if there was no bone attrition and 4b if there was any subchondral bone attrition. To determine knee alignment, the angle between a line connecting the centre of the femoral head and the line connecting the centre of the knee to the centre of the ankle was measured. The lateral/skyline radiographs were only used to record an overall assessment of the presence or absence of patella-femoral joint OA. A similar overall judgement was made of the presence or absence of both medial and lateral compartment OA on the AP films allowing categorisation of compartmental involvement in each knee joint. In addition, osteophyte scores in each compartment were evaluated separately, as the mK–L score does not account for osteophyte severity.

Surgery

All patients underwent a fully cemented non-constrained TKR. Procedures were performed by a team of surgeons using implants purchased from four manufacturers only. Individual surgeons did not alter their manufacturer or implant types during the study time frame.

Main independent variables

The main predictor variable was overall radiographic OA severity using the modified K–L grade (mK–L) with grades 1 & 2 collapsed into a single category (K–L <3) due to small numbers ($n = 15$). In addition, osteophyte scores were included in initial univariate analyses.

Outcome variables

The outcome variables were the IKSS pain and function scores at 12 and 24 months. We evaluated the relationship between the main independent variable (radiographic OA severity, osteophyte scores and pre-operative mechanical axis) and outcome variables (pain and function score), adjusting for the compartment involved and clinically relevant covariates.

Covariates

Multivariable regression analyses were adjusted for gender, baseline age, body mass index (BMI) and age-adjusted Charlson Co-morbidity Index (CCI)[34]. Other covariates included baseline pain and function scores and SF12 mental and physical function scores. Surgical variables included in the models were patella resurfacing and the type of prosthesis, namely cruciate retaining, posterior stabilising or ultra-congruent.

Statistical analysis

Summary statistics [mean, standard deviation (+/−SD) and percentage (%)] are presented for demographic and clinical characteristics of the study cohort. Separate multivariable linear regression models were created to evaluate the relationship between the mK–L grade and pain and function subscales of the IKSS, measured on a continuous scale, at 12 months and 2 years. We dichotomised pain into two categories based on severity at 12 months and 2 years (those with IKSS pain score ≥30 were classified as having none to mild pain and those with IKSS pain score <30 were classified as having moderate to severe pain[24]. We also dichotomised function into two categories (those with an IKSS function score ≥60) were classified as having a fair to excellent functional outcome and those with an IKSS function score <60 as having a poor functional outcome[35]. Cut-off scores for these outcomes were based on the IKSS system which rates pain as follows; no pain (50), mild occasional pain (45) mild pain on stairs (40), mild pain on walking (30), moderate occasional pain (20), moderate continual pain (10) and severe pain as (0) points. Further, ratings for function are classified as; excellent (80–100), good (70–79), fair (60–69), and less than 60 poor.[35] Adjusted logistic regression was used to determine the odds ratio (OR) of having ongoing moderate to severe pain or poor function at 12 months and 2 years post TKR, for each modified KL grade, using K–L 4b as the reference point. For regression analyses, X-rays were categorised as showing nil/uni-compartmental OA changes, or multi-compartmental changes. Statistical significance was defined as $p \leq 0.05$.

Analyses were performed using SPSS for Windows version 18.0 (SPSS Inc., Chicago, Illinois). STATA Version 11.1 (StataCorp, College Station, Texas, USA) was used to generate the figures.

Results

Study cohort and follow-up

A total of 557 primary knee replacements were performed for OA in 525 enrolled patients during the study period. No simultaneous bilateral TKRs were performed, and in those patients who underwent staged bilateral joint replacement, only the second procedure was included in the analysis. Twenty-four patients were excluded as they underwent uni-compartmental knee replacement and 23 radiographs were rejected because of technical problems (16) or because no film was available within 6 months of surgery (7), leaving 478 TKR's for inclusion. Five patients did not return questionnaires at 12 months due to: deceased ($n = 3$), cognitive impairment ($n = 1$), declined ($n = 1$), and a further 26 patients at 2 years due to: deceased ($n = 8$), underwent revision knee replacement ($n = 5$), declined ($n = 7$), lost to follow-up ($n = 4$), overseas ($n = 2$). Therefore follow-up pain and function data were available for analysis in 473 of 478 (99.4%) patients at 12 months and 447 of 478 (93.5%) patients at 2 years following TKR. Given the high follow-up rate, non-responder analysis was not performed.

Demographic and clinical characteristics of the cohort are presented in Table I. There were 478 patients with a mean age of 70.8 (SD +/−8.3) years. Three hundred and thirty one (69.2%) were female and the mean BMI was 32.2 (+/− 6.0) kg/m^2.

Pain scores improved from a pre-operative mean of 4.0 (+/−7.3) to 34.9 (+/− 15.4) at 12 months and 34.8 (+/− 15.9) at 2 years. However, when pain was dichotomised into two groups (based on IKSS pain score ≥30 or <30), 140 of 474 (29.5%) patients at 12 months and 137 of 448 (30.6%) patients at 2 years still had moderate to severe pain. The mean pre-operative function score was 37.5 (+/− 18.1) improving to 58.8 (+/− 25.0) at 12 months and 55.5 (+/− 26.8) at 2 years (maximum function score being 100 points). When function was dichotomised into two groups (based on IKSS function score ≥ 60 or <60), 232 of 474 (48.9%) patients at 12 months, and 227 of 448 (50.7%) patients at 2 years rated their function as poor.

Table I
Patient characteristics

Variable		Mean ± SD, or n(%)	Median	Minimum, maximum
Age (years)		70.8 ± 8.3	71.5	45.0, 90.0
BMI (kg/m^2) *		32.2 ± 6.0	31.6	17.4, 50.6
Age-adjusted CCI †		1.9 ± 2.2	0.0	0.0, 7.0
Pre-op SF12 PCS ‡		26.2 ± 5.6	25.3	39.9, 54.4
Pre-op SF12 MCS **		50.6 ± 10.7	52.5	18.4, 71.3
Pre-op Pain Score ††		4.0 ± 7.3	0.0	0.0, 45.0
12 month Pain Score ††		34.9 ± 15.4	45.0	0.0, 50.0
2 year Pain Score ††		34.8 ± 15.9	45.0	0.0, 50.0
Pre-op Function Score ‡‡		37.5 ± 18.1	35.0	0.0, 100.0
12 month Function Score ‡‡		58.8 ± 25.0	60.0	0.0, 100.0
2 year Function Score ‡‡		55.5 ± 26.8	55.0	0.0, 100.0
Gender	Male	147 (30.8%)		
	Female	331 (69.2%)		
Side	Right	276 (57.7%)		
	Left	202 (42.3%)		
Prosthesis Type	Cruciate retaining	197 (41.2%)		
	Posterior stabilising	267 (55.9%)		
	Ultra congruent	14 (2.9%)		
Patella Resurfaced	Yes	153 (32.0%)		
	No	325 (68.0%)		
Modified Kellgren and Lawrence grade	<3	15 (3.1%)		
	3a	57 (11.9%)		
	3b	200 (42.1%)		
	4a	87 (18.2%)		
	4b	119 (24.9%)		
OA Compartment	No Definite	6 (1.3%)		
	Medial Only	104 (21.8%)		
	Lateral Only	37 (7.7%)		
	Medial and PF	244 (51.0%)		
	Lateral and PF	40 (8.4%)		
	PF only	9 (1.9%)		
	Medial and Lateral	6 (1.3%)		
	Tricompartmental	31 (6.5%)		
Multi-compartmental OA	Yes	322 (67.4%)		
	No	155 (32.4%)		
Medial Osteophyte Score	0	53 (11.1%)		
	1	182 (38.1%)		
	2	211 (44.1%)		
	3	32 (6.7%)		
Lateral Osteophyte Score	0	45 (9.4)		
	1	234 (49.0)		
	2	176 (36.8%)		
	3	23 (4.8%)		

* BMI (weight [Kg]/height [m]^2).
† CCI (0–43, age adjusted), with a higher score indicating a greater comorbidity burden.
‡ SF12 PCS – Short Form 12 PCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
** SF12 MCS – Short Form 12 MCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
†† IKSS pain score ranges from 0 to 50, with higher scores indicating less pain (0 = maximum pain, 50 = no pain).
‡‡ IKSS function score ranges from 0 to 100, with higher scores indicating better function.

Radiographic findings

The intra-rater reliability scores demonstrated substantial reproducibility. The intra-rater kappa value for the K–L grade was 0.69, and for JSN 0.70 (medial JSN) and 0.80 (lateral JSN). For the attrition score kappa values were 0.74 (medial) and 0.84 (lateral), and for osteophyte scores 0.69 (medial) and 0.65 (lateral). The kappa values for compartments were as follows: 1.0 (no definite OA), 0.89 (medial OA), 0.78 (lateral OA), and 0.65 (patello-femoral OA).

Figure 1 shows the frequency of the mK–L radiographic grades [Fig. 1(a)] and compartments involved [Fig. 1(b)]. The majority of patients with K–L grade 3 had significant JSN (category 3b), while more than half of those with K–L grade 4 OA, also had evidence of bone attrition (category 4b).

Predictors of pain outcome

Pre-operatively, most patients reported severe pain irrespective of radiographic OA severity or compartmental involvement. Post-operatively, there were proportionately more patients with mild or no pain, compared with pre-op, regardless of radiographic OA severity or compartment. Mean (SD) pre and post-operative pain scores for each modified K&L grade and compartment involvement are provided in Supplementary Tables. In univariate analyses higher IKSS pain scores at 12 and 24 months were associated with greater pre-operative mK–L grade and multicompartment OA involvement. However there were no associations between these radiographic OA features and pre-operative pain scores (Supplementary Tables).

Results of linear regression modelling for independent determinants of IKSS pain scores are presented in Table II. Higher pre-operative pain scores were associated with higher pre-operative IKSS function scores and with higher SF12 scores, but not with radiographic severity. The determinants of pain post-operatively included lower baseline SF12 MCS, a cruciate retaining prosthesis, greater pre-operative mK–L grade, and multi-compartmental involvement (24 months only). There were no consistent association between the presence and size of osteophytes nor pre-operative mechanical axis, so they were not included in multivariable regression models. The multivariable logistic regression analysis (Table III) demonstrated significantly higher odds of ongoing moderate to severe pain for patients with less severe radiographic changes (most consistently mK–L grades ≤3a). Poorer pre-operative mental health (lower baseline MCS) and a higher age-adjusted CCI also significantly increased the odds of ongoing moderate to severe pain post TKR, whereas use of a cruciate retaining prosthesis reduced the likelihood of pain and multi-compartmental radiographic involvement had no effect.

Predictors of functional outcome

In contrast to pain severity patients had a broader range of functional impairment, though the majority had poor function as manifest in an IKSS function score <60. Post-operatively, there was an overall shift towards improved function among patients of all mK–L severity grades. Mean (SD) pre and post-operative IKSS function scores for each modified K&L grade and compartment involvement are provided in Supplementary Tables. In univariate analyses, associations between IKSS function scores at 12 and 24 months with pre-operative mK–L grade and multicompartment OA involvement were inconsistent. Logistic regression demonstrated higher odds of poor function at 12 months only for individuals with an mK–L grade of 3a and 4a compared to 4b. Linear regression demonstrated an association between multicompartment OA and lower pre-operative function scores (Supplementary Tables).

Results of linear regression modelling for independent determinants of IKSS function scores are presented in Table IV. Older age, female gender and age-adjusted CCI were significant predictors of poorer pre-op IKSS function scores. Higher baseline pain score, SF12 PCS and MCS were also significant predictors of higher pre-operative IKSS function scores.

Postoperatively (Table V) older age, female gender, higher baseline BMI, and worse physical and mental function pre-operatively were all significant predictors of poorer IKSS function scores post TKR. Pre-operative radiographic OA severity and compartmental involvement did not predict functional outcomes at either time point after TKR in linear regression modelling. Subsequent multivariable logistic regression demonstrated significantly higher odds of reporting poor function for patients with modified K-L grades of 3a and 4a when compared to 4b at 12 months post TKR, but there were no associations between function and mK–L at 24 months. Older age, female gender, and higher BMI significantly increased the odds of reporting poor function post-operatively, as did poorer pre-operative function and mental health (lower pre-operative IKSS function scores and SF12 PCS or MCS), whereas the use of a cruciate retaining prosthesis reduced those odds.

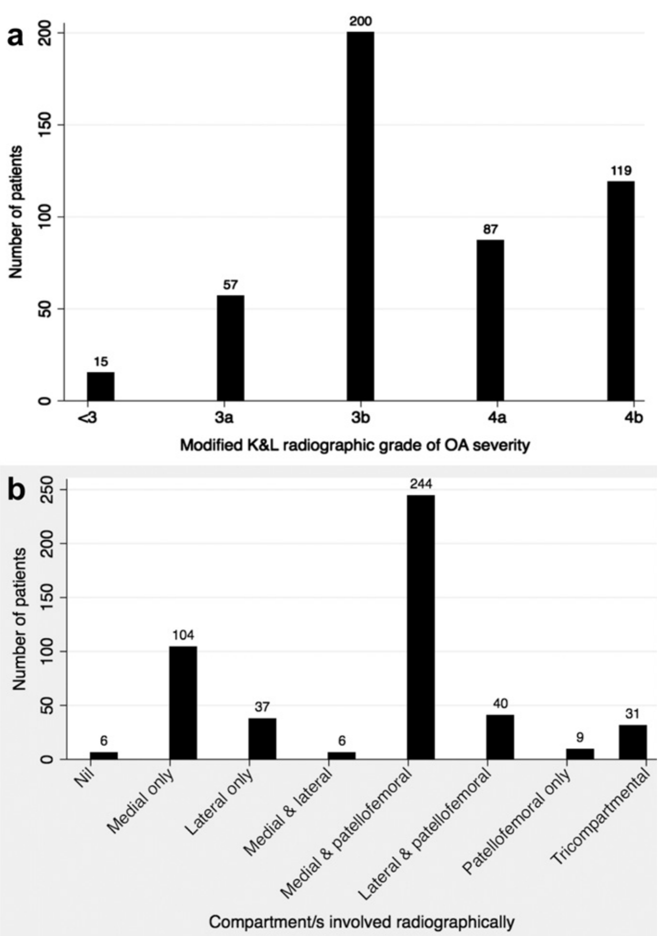

Fig. 1. Frequency bar graphs for modified Kellgren & Lawrence (mK–L) grade of radiographic knee OA severity (1a) and knee compartments involved radiographically (1b).

Discussion

The main new finding of this study is that people with less severe radiographic changes prior to knee joint replacement are less likely to experience major improvement in pain and function 1 and 2 years post-operatively than those with more severe changes. Further, our findings suggest that radiographic severity of OA may be a more robust determinant of functional outcomes at 12 months than at 24 months. The distribution of the osteoarthritic changes within the joint (medial or lateral tibio-femoral and the patella-

Table II
Multivariable-adjusted association of modified K&L grade with pain score

Variable	Pre-op		12 months		2 years	
	B (95% CI)	*P*	B (95% CI)	*P*	B (95% CI)	*P*
Age	0.06 (−0.03–0.14)	0.174	0.14 (−0.05–0.32)	0.143	0.18 (−0.02–0.37)	0.074
Female	−0.89 (−2.36–0.56)	0.228	−1.56 (−4.69–1.57)	0.327	−1.87 (−5.13–1.38)	0.258
BMI †	0.03 (−0.08–0.14)	0.607	−0.11 (−0.35–0.13)	0.352	−0.14 (−0.39–0.12)	0.289
Age-adjusted CCI ‡	−0.05 (−0.36–0.26)	0.751	−0.45 (−1.11–0.21)	0.184	−0.60 (−1.30–0.10)	0.091
Pre Knee Pain Score ‡‡	–	–	0.14 (−0.06–0.33)	0.169	0.13 (−0.07–0.33)	0.214
Pre Function Score ***	0.06 (0.02–0.10)	**0.004**	0.05 (−0.04–0.13)	0.299	0.01 (−0.08–0.10)	0.873
Pre SF12 PCS **	0.40 (0.28–0.52)	**<0.001**	0.25 (−0.02–0.52)	0.067	0.27 (−0.00–0.55)	0.054
Pre SF12 MCS ††	0.07 (0.00–0.13)	**0.037**	0.22 (0.09–0.36)	**0.002**	0.36 (0.22–0.50)	**<0.001**
Cruciate Retaining	–	–	4.63 (1.64–7.63)	**0.002**	4.25 (1.11–7.40)	**0.008**
Patella Resurfaced	–	–	1.60 (−1.49–4.69)	0.309	2.03 (−1.22–5.28)	0.220
Modified K-L grade *	−0.15 (−0.75–0.45)	0.623	2.11 (0.80–3.42)	**0.002**	2.13 (0.76–3.50)	**0.002**
Multi-compartmental OA	−0.19 (−1.57–1.20)	0.790	2.47 (−0.54–5.48)	0.108	3.14 (0.29–6.25)	**0.048**

* Beta coefficient represents the magnitude of change in pain score with each worsening mK–L grade.
† BMI (weight [Kg]/height [m]^2).
‡ CCI (0–43, age adjusted), with a higher score indicating a greater comorbidity burden.
** SF12 PCS – Short Form 12 PCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
†† SF12 MCS – Short Form 12 MCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
‡‡ IKSS pain score ranges from 0 to 50, with higher scores indicating less pain (0 = maximum pain, 50 = no pain).
*** IKSS function score ranges from 0 to 100, with higher scores indicating better function.
Bold denotes statistical significance.

femoral compartments) makes relatively little difference, and the degree of pre-operative osteophytosis seems unimportant to outcome, but the amount of damage to the articular cartilage (as judged by radiographic JSN) and subchondral bone (assessed as bone attrition from radiographs) do determine outcomes. Severe pre-operative X-ray changes are predictive of a good outcome.

Other determinants of outcomes apparent from these data include age, gender, obesity, co-morbidities, and pre-operative pain, functional status and mental health status, and it is interesting to note that these determinants appear to have different effects on pain and function. People with more co-morbidities and those who have worse pain, function and mental health pre-operatively are less likely to gain in terms of either function or pain. In contrast, age, gender and obesity only influenced functional outcomes, and not pain, with older people, women and the obese experiencing poorer functional outcomes. We also examined the potential influence of the type of prosthesis used and found that while the presence or absence of patella resurfacing appeared to have no effect, the use of a cruciate retaining prosthesis was associated with better outcomes.

Table III
Multivariable-adjusted association of modified K&L with moderate to severe pain

Variable	12 months		2 years	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	0.98 (0.95–1.01)	0.186	0.98 (0.95–1.01)	0.148
Female	1.32 (0.79–2.20)	0.288	1.26 (0.75–2.14)	0.384
BMI†	1.00 (0.97–1.04)	0.822	1.03 (0.99–1.07)	0.122
Age-adjusted CCI ‡	1.12 (1.00–1.24)	**0.043**	1.11 (0.99–1.24)	0.077
Pre knee pain score ‡‡	0.98 (0.94–1.01)	0.191	0.98 (0.95–1.02)	0.267
Pre function score ***	1.00 (0.98–1.01)	0.501	1.01 (0.99–1.02)	0.540
Pre SF12 PCS **	0.97 (0.93–1.02)	0.223	0.97 (0.93–1.02)	0.238
Pre SF12 MCS ††	0.97 (0.95–1.00)	**0.014**	0.95 (0.93–0.97)	**<0.001**
Cruciate retaining	0.51 (0.31–0.83)	**0.007**	0.54 (0.32–0.90)	**0.019**
Patella resurfaced	0.84 (0.50–1.39)	0.488	0.70 (0.41–1.20)	0.196
Modified K–L <3 *	5.39 (1.23–15.69)	**0.023**	2.17 (0.58–8.13)	0.250
Modified K–L 3a*	2.62 (1.21–5.67)	**0.015**	2.77 (1.26–6.10)	**0.011**
Modified K–L 3b*	1.81 (1.00–3.26)	**0.049**	1.63 (0.90–2.92)	0.104
Modified K–L 4a*	2.06 (1.05–4.05)	**0.036**	0.87 (0.42–1.80)	0.824
Multi-compartmental OA	0.81 (0.50–1.30)	0.388	0.62 (0.38–1.01)	0.055

* Reference = Modified K–L 4b.
† BMI (weight [Kg]/height [m]^2).
‡ CCI (0–43, age adjusted), with a higher score indicating a greater comorbidity burden.
** SF12 PCS – Short Form 12 PCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
†† SF12 MCS – Short Form 12 MCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
‡‡ IKSS pain score ranges from 0 to 50, with higher scores indicating less pain (0 = maximum pain, 50 = no pain).
*** IKSS function score ranges from 0 to 100, with higher scores indicating better function.
Bold denotes statistical significance.

Many of these findings are consistent with existing literature. As noted in the introduction, several other studies have found that significant numbers of people who have had a TKR continue to complain of pain in the operated knee in the intermediate period (1–10 years) after surgery, in the absence of an obvious cause for that pain[13,36]. About 30% of our group of patients had moderate or severe pain in the replaced knee 1 and 2 years after surgery, a figure that is similar to those quoted by Wylde *et al.*[36] and Beswick *et al.*[13]. Other groups have also described similar determinants of poor outcomes after TKR; for example, age, gender, obesity and other co-morbidities, as well as pre-operative pain, physical function and mental state, have all been found to be determinants of some of the variation of outcomes in other cohorts[3,10,14–18,36].

However, there have been very few other investigations of the influence of pre-operative radiographic features on TKR outcomes; we are only aware of two other reports. In 2008 Cushnaghan *et al.* published data from a prospective case–control study of 657 matched pairs of patients and controls undergoing TKR; they found that X-ray severity, defined by the simple Kellgren and Lawrence score, had a small effect in the same direction that we observed (i.e., those with worse X-rays having better outcomes), that did not reach statistical significance[21]. This study had a number of acknowledged limitations, most notably a large loss of patients over time. More recently Valdes *et al.* have published data from a study of 868 post-TKR patients[20]. They found that both Kellgren and Lawrence scores and specific assessment of JSN influenced outcomes, and again showed that those with the worst pre-operative X-ray findings had the best outcome, with more effect seen on pain than on function [using the Western Ontario and McMaster Universities Arthritis Index (WOMAC) score as the outcome measure]. The main limitations to this study were the fact that it was a retrospective and cross sectional study, in which pre-operative clinical data were not available. However, considering our data alongside that of Cushnaghan *et al.* and Valdes *et al.*[20,21], and

Table IV
Multivariable-adjusted association of modified K&L with function score

Variable	Pre-op		12 months		2 years	
	B (95% CI)	*P*	B (95% CI)	*P*	B (95% CI)	*P*
Age	−0.43 (−0.62–0.24)	**<0.001**	−0.43 (−0.69–0.18)	**0.001**	−0.66 (−0.96–0.38)	**<0.001**
Female	−8.17 (−11.42–4.91)	**<0.001**	−5.78 (−10.22–1.34)	**0.011**	−8.86 (−13.73–4.00)	**<0.001**
BMI†	−0.08 (−0.33–0.18)	0.546	−0.79 (−1.13–0.46)	**<0.001**	−0.78 (−1.15–0.40)	**<0.001**
Age-adjusted CCI‡	−1.01 (−1.70–0.31)	**0.005**	−0.68 (−1.62–0.26)	0.154	−1.11 (−2.16–0.07)	**0.037**
Pre Knee Pain Score ‡‡	0.30 (0.10–0.51)	**0.004**	−0.13 (−0.41–0.15)	0.350	0.00 (−0.30–0.31)	0.980
Pre Function Score***	–	–	0.43 (0.31–0.55)	**<0.001**	0.40 (0.26–0.53)	**<0.001**
Pre SF12 PCS**	0.64 (0.36–0.92)	**<0.001**	0.69 (0.31–1.07)	**<0.001**	0.67 (0.25–1.09)	**0.002**
Pre SF12 MCS††	0.46 (0.33–0.60)	**<0.001**	0.47 (0.27–0.66)	**<0.001**	0.47 (0.26–0.68)	**<0.001**
Cruciate Retaining	–	–	4.08 (−0.16–8.33)	0.060	2.81 (−1.90–7.52)	0.241
Patella Resurfaced	–	–	1.78 (−2.60–6.17)	0.426	0.98 (−3.88–5.84)	0.692
Modified K-L*	−0.08 (−1.29–1.46)	0.907	1.24 (−0.63–3.10)	0.193	0.98 (−1.07–3.02)	0.349
Multi-compartmental OA	−2.92 (−6.08–0.25)	0.071	−0.69 (−4.96–3.58)	0.751	1.34 (−3.32–6.00)	0.572

* Beta coefficient represents the magnitude of change in pain score with each worsening mK–L grade.
† BMI (weight [Kg]/height [m]^2).
‡ CCI (0–43, age adjusted), with a higher score indicating a greater comorbidity burden.
** SF12 PCS – Short Form 12 PCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
†† SF12 MCS – Short Form 12 MCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
‡‡ IKSS pain score ranges from 0 to 50, with higher scores indicating less pain (0 = maximum pain, 50 = no pain).
*** IKSS function score ranges from 0 to 100, with higher scores indicating better function.
Bold denotes statistical significance.

similar findings from studies of total hip replacement[37,38], we conclude that there is a definite inverse relationship between pre-operative radiographic severity of OA, and intermediate-term outcomes after joint replacement.

Our study has both strengths and limitations. Its great strength is the fact that it is a large, inclusive prospective study in which there have been almost no losses to follow-up or missing data. As noted by Murray *et al.*, orthopaedic follow-up studies are beleaguered by selection issues and especially by differential loss to follow-up, making it virtually impossible to conclude who gets the best or worst outcomes and why[39]. Although geographically limited, this study has none of those limitations. Another strength of our study, is the fact that the radiographs were read by a single observer with proven good reproducibility of his findings, using standard atlases and techniques. However, an arguable weakness is the use of the IKSS as the only condition specific measure of joint pain. The IKSS does not clearly differentiate pain severity from function-related pain, and does not account for rest pain, night pain or intermittent attacks of pain. Another potential weakness is the fact that this is a single site study based in a tertiary referral centre in one Australian city, meaning that the results may have limited generalisability. We were unable to adjust for all potential confounders, most notably several clinical variables such as prosthesis type, surgeon experience and load bearing distribution at the knee. However, surgery at our institution is standardised and all patients underwent a fully cemented fixed-bearing, non-constrained TKR. While an association between surgeon experience and component positioning has been demonstrated[40] this finding has not borne out in larger series[41]. Abnormal load transfer as a consequence of malalignment post TKR is a risk factor for component failure in the longer term[42]. However there is limited but contrasting literature regarding load distribution and pain and function post TKR in the short to midterm[43,44].

Table V
Multivariable-adjusted association of modified K&L with poor function

Variable	12 months		2 years	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	1.07 (1.03–1.10)	**<0.001**	1.08 (1.04–1.12)	**<0.001**
Female	1.81 (1.08–3.03)	**0.025**	2.06(1.20–3.53)	**0.009**
BMI†	1.07 (1.03–1.12)	**<0.001**	1.09 (1.05–1.14)	**<0.001**
Age-adjusted CCI‡	1.05 (0.94–1.17)	0.406	1.18 (1.05–1.33)	**0.005**
Pre knee pain score‡‡	1.01 (0.97–1.04)	0.759	1.02 (0.99–1.06)	0.238
Pre function score***	0.96 (0.95–0.98)	**<0.001**	0.97 (0.95–0.98)	**<0.001**
Pre SF12 PCS**	0.91 (0.87–0.96)	**<0.001**	0.94 (0.90–0.99)	**0.014**
Pre SF12 MCS††	0.95 (0.92–0.97)	**<0.001**	0.94 (0.92–0.97)	**<0.001**
Cruciate retaining	0.58 (0.35–0.95)	**0.032**	0.73 (0.44–1.23)	0.244
Patella resurfaced	0.95 (0.57–1.59)	0.853	0.96 (0.56–1.64)	0.870
Modified K–L <3*	1.55 (0.40–6.05)	0.532	3.28 (0.68–15.85)	0.139
Modified K–L 3a*	2.81 (1.23–6.39)	**0.014**	1.65 (0.70–3.84)	0.250
Modified K–L 3b*	1.47 (0.82–2.62)	0.195	1.04 (0.57–1.89)	0.903
Modified K–L 4a*	2.45 (1.22–4.91)	**0.011**	1.46 (0.72–2.96)	0.300
Multi-compartmental OA	0.78 (0.47–1.29)	0.328	0.88 (0.53–1.48)	0.631

* Reference = Modified K-L 4b.
† BMI (weight [Kg]/height [m]^2).
‡ CCI (0–43, age adjusted), with a higher score indicating a greater comorbidity burden.
** SF12 PCS – Short Form 12 PCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
†† SF12 MCS – Short Form 12 MCS of ≥50 indicates no impairment; 40–49 mild impairment; 30–39 moderate impairment; and <30 severe impairment.
‡‡ IKSS pain score ranges from 0 to 50, with higher scores indicating less pain (0 = maximum pain, 50 = no pain).
*** IKSS function score ranges from 0 to 100, with higher scores indicating better function.
Bold denotes statistical significance.

There are two findings from our data that we think are worthy of further comment and interpretation. First we have shown that the outcomes for pain and function after a TKR may have different determinants. This may not have been made apparent from previous studies because of the widespread use of single ‘algofunctional’ outcomes data as the total WOMAC or Lequesne index scores, and could be important when it comes to considering the indications for surgery and discussing likely outcomes with patients. We believe that the most likely reason for this differentiation is the fact that function depends on all other joints and systems, and not just on the one knee that is being replaced, whereas the pain assessment is specifically related to pain in that one joint.

The second finding that needs comment is the main new discovery that the severity of the pre-operative radiographic joint damage is inversely related to the chances of a good outcome, and that this is more obvious for pain than it is for function. Again, this could have important implications for surgical decision making, and taking this finding alongside the other data presented and the existing literature, we believe that surgeons should be particularly wary of operating on patients with a lot of joint pain but modest X-ray damage, particularly if they have other concomitant psychosocial or medical problems. Conversely, surgeons and their patients do not need to be influenced by the distribution of the changes within the joint, or the degree of osteophyte formation, when making the important decision as to whether it is appropriate to undertake a TKR. But, in addition to its clinical implications, the finding requires explanation – why is it that patients with modest X-ray changes do not do so well? The explanation put forward by Valdes *et al.* is that pain central sensitisation might be a more important cause of severe pain in those with milder joint damage compared to those with severe damage, in whom a large amount of the pain experience is driven directly by nocioceptive input from the joint[20]. This is certainly consistent with recent findings in the field, which include a high prevalence of features of pain sensitisation in OA patients[45–47], and with the finding that 'pain elsewhere' is also common in some patients with OA [36]. This potential explanation needs further evaluation, as it maybe that some sort of screening test should be carried out pre-operatively in order to ascertain the degree of central pain sensitisation, and attempts made to treat this, prior to TKR. There are alternative explanations, such as exposure to different types of pain interventions for different lengths of time that should also be considered.

In conclusion we have shown that there is an inverse relationship between the severity of pre-operative radiographic changes and post-operative pain and function in people undergoing primary TKR for OA, and suggest that this has important clinical implications in patient selection, as well as requiring explanation through further research.

Contributions

Conception and design: Dowsey, Nikpour, Dieppe, Choong.
Analysis and interpretation of the data: Dowsey, Nikpour, Dieppe, Choong.
Drafting of the article: Dowsey, Nikpour, Dieppe.
Critical revision of the article for important intellectual content: Dowsey, Nikpour, Dieppe, Choong.
Final approval of the article: Dowsey, Nikpour, Dieppe, Choong.
Provision of study materials or patients: Dowsey, Choong.
Statistical expertise: Dowsey, Nikpour.
Collection and assembly of data: Dowsey, Nikpour, Dieppe, Choong.

Declaration

Dr Dowsey had full access to all of the data in the study and takes responsibility for the integrity of the work as a whole, from inception to finished article – email: mmdowsey@unimelb.edu.au.

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Competing interest statement
None of the authors have any financial or personal relationships with other people or organisations that could potentially and inappropriately influence their work and conclusions.

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2. Prof Choong receives consultancy fees from DePuy for being part of education faculties.
3. Prof Choong is part of a surgeon design team for which he receives consultancy fees from DePuy for time spent.
4. Prof Choong receives royalties from Zimmer for tumour prosthesis design.

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Supplementary material

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